In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

No. 14-439V

(to be published)

LEIGH ROLSHOVEN, *as the court-appointed Guardian and Conservator of* HANNAH HUELSENBECK,	*	
Petitioner,	*	Filed: January 11, 2018
v.	*	Decision; Entitlement; Dismissal of Claim; Human Papillomavirus ("HPV") Vaccine; Idiopathic Intracranial Hypertension ("IIH"); Pseudotumor Cerebri ("PC").
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	
Respondent.	*	

Mark Sadaka, Mark T. Sadaka, LLC, Englewood, NJ, for Petitioner.

Debra A. Filteau Begley, U.S. Dep't of Justice, Washington, DC, for Respondent.

DECISION[1]

On May 22, 2014, Ms. Leigh Rolshoven, legal guardian of Hannah Huelsenbeck, filed this action seeking compensation under the National Vaccine Injury Compensation Program (the "Vaccine Program").[2] The Petition alleges that Ms. Huelsenbeck developed psuedotumor cerebri/idiopathic intracranial hypertension ("IIH")[3], persistent/chronic headaches, and other

[1] Because this Decision has been formally designated "to be published," it will be posted on the Court of Federal Claims's website in accordance with the E-Government Act of 2002, 44 U.S.C. § 3501 (2012). **This means the ruling will be available to anyone with access to the internet**. As provided by 42 U.S.C. § 300aa-12(d)(4)(B), however, the parties may object to the Decision's inclusion of certain kinds of confidential information. Specifically, under Vaccine Rule 18(b), each party has fourteen days within which to request redaction "of any information furnished by that party: (1) that is a trade secret or commercial or financial in substance and is privileged or confidential; or (2) that includes medical files or similar files, the disclosure of which would constitute a clearly unwarranted invasion of privacy." Vaccine Rule 18(b). Otherwise, the Decision in its present form will be available to the public. *Id.*

[2] The Vaccine Program comprises Part 2 of the National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3758, codified as amended at 42 U.S.C. §§ 300aa-10 through 34 (2012) ("Vaccine Act" or "the Act"). Individual section references hereafter will be to § 300aa of the Act (but will omit that statutory prefix).

[3] Pseudotumor cerebri and IIH are largely interchangeable diagnostic descriptions of the same condition.

adverse reactions due to the receipt of a second dose of the human papillomavirus ("HPV" or "Gardasil") vaccine on August 5, 2011. Petition ("Pet.") (ECF No. 1) at 1.

An entitlement hearing in the matter was held on May 11-12, 2017. After considering the record as a whole, and for the reasons explained below, I find that Petitioner has not carried her burden establishing causation. The facts of this case do not support the conclusion that any of the HPV doses Ms. Huelsenbeck received were "more likely than not" causal of her headaches or IIH. Moreover, Petitioner's causation theory was wholly unreliable.

Factual Background

HPV Vaccination and Immediate Symptoms

On August 5, 2011, Ms. Huelsenbeck received her second HPV vaccination. Ex. 2 at 12. She had received her first (in a series of three doses) six weeks before, on June 27, 2011, but experienced no documented reaction to it. *Id.* At the time of these vaccinations, Ms. Huelsenbeck (who was then 16 years old) had a history of attention/defect hyperactivity disorder ("ADHD")[4], and had struggled socially and academically for a number of years. *See, e.g.*, Ex. 24 at 47; Ex. 20 at 17, 50, 101, 176, 262; Pet. at 1. In addition, Ms. Huelsenbeck's medical records suggest that she had previously suffered from "severe headaches" and "vision problems," beginning as early as October 2006. Ex. 24 at 28.

There is some subsequent medical record evidence of post-vaccination symptoms. On August 29, 2011, Petitioner brought Ms. Huelsenbeck to her primary care provider ("PCP"), Dr. Steven Hartberg, reporting that Ms. Huelsenbeck had been suffering from a constant headache for the past two weeks (or since August 15th – ten days after the second HPV dose). Ex. 2 at 11. Ms. Huelsenbeck described these headaches as increasing throughout the day, limited to the left side of her head but worsening when she bent over. *Id.* She was assessed to be suffering from migraines and prescribed Maxalt, an anti-nausea medication.[5]

[4] Attention-deficit/hyperactivity disorder ("ADHD") is a chronic condition resulting in a variety of symptoms, including inattention, hyperactivity, and impulsive behavior. *Attention-deficit/hyperactivity disorder (ADHD) in children*, Mayo Clinic, https://www.mayoclinic.org/diseases-conditions/adhd/symptoms-causes/syc-20350889 (last visited Oct. 23, 2017).

[5] Maxalt is a trademark for Rizatriptan. *Dorland's Illustrated Medical Dictionary* 1114 (32nd ed. 2012) (hereinafter *Dorland's*). Maxalt or Rizatriptan is used to treat acute migraines in adults and children. *Rizatriptan (Oral Route)*, Mayo Clinic, https://www.mayoclinic.org/drugs-supplements/rizatriptan-oral-route/description/DRG-20065868 (last visited Oct. 23, 2017). It can also be used to treat nausea, vomiting, light sensitivity, and sensitivity to sound. *Id.* Maxalt is typically prescribed when aspirin or other pain relievers prove ineffective. *Id.*

The next medical record is from October 21, 2011, when Ms. Huelsenbeck saw Dr. Terry Lang (the physician responsible for treating her pre-existing ADHD), at which time she discussed her then-current academic and personal issues. Ex. 20 at 287. A full physical exam was performed, but Ms. Huelsenbeck noted no concerns about the headaches she now alleges to have experienced in August. A month later, on November 10, 2011, Ms. Huelsenbeck received a mental health assessment at Sioux Trails Mental Health Center at the recommendation of her high school. Ex. 24 at 36. Her history of ADHD and other behavioral/psychological problems was noted, and she was diagnosed as clinically depressed, with symptoms related to anxiety. *Id.* Again, however, the records from this visit (now nearly three months from the date of the second HPV dose) do not reference any complaints of headaches.

Increase in Headache Severity

On November 29, 2011, Ms. Huelsenbeck returned to Dr. Hartberg, again complaining of recurring headaches that spiked under certain circumstances but which could be alleviated by taking a hot shower. Ex. 2 at 10. She was assessed with a probable migraine, and the doctor's notes from this visit linked her current symptoms to her earlier visit to Dr. Hartberg in August for similar complaints. *Id.* A month later, on December 18, 2011, Petitioner accompanied Ms. Huelsenbeck to the emergency room ("ER"), reporting that Ms. Huelsenbeck had been suffering from a "headache for about a month," and had missed school on many days as a result. Ex. 4 at 1, 13. A head CT scan was negative. *Id.* at 3. Ms. Huelsenbeck was administered an injection of Toradol[6] and discharged with pain medication. *Id*. at 14.

Unfortunately, Ms. Huelsenbeck's headaches persisted thereafter. She thus returned to her PCP on December 20, 2011, with similar complaints from the two days before plus nausea. Ex. 2 at 10. She was diagnosed again with a migraine headache and given Maxalt plus pain medication. *Id.* Three days later, during a follow-up with Dr. Hartberg on December 23, 2011, Ms. Huelsenbeck reported that her headaches had completely resolved. *Id.* at 9. And toward the end of December, when Ms. Huelsenbeck again saw Dr. Lang for her ADHD, Petitioner informed Dr. Lang of the ongoing headaches, reporting that they were getting worse over the past month despite treatment with over-the-counter pain relievers. Ex. 20 at 307. Consistent with other treaters who had seen Ms. Huelsenbeck over the prior five months, Dr. Lang proposed that the headaches were most likely migraines, and he prescribed pain medication (in addition to Adderall for her ADHD). *Id.*

[6] Toradol is a trademark for ketorolac tromethamine. *Dorland's* at 1940. Toradol is a nonsteroidal anti-inflammatory drug (NSAID) used to treat moderately severe pain, and is sometimes used in combination with other pain relievers to relieve pain. *Ketorolac (Oral Route, Injection Route)*, Mayo Clinic, https://www mayoclinic.org/drugs-supplements/ketorolac-oral-route-injection-route/description/drg-20066882 (last visited Oct. 23, 2017).

Third HPV Vaccine Dose

Right before New Year's Eve, on December 30, 2011, Ms. Huelsenbeck received her third HPV vaccine dose and her second Hepatitis A vaccine. Ex. 2 at 9. There is no record evidence of an immediate reaction to this final HPV dose, however, or any further headaches in January 2012.

On February 1, 2012 (now over a month since the third HPV dose), Ms. Huelsenbeck went back to Dr. Hartberg, again complaining of headaches, along with nausea, dry heaves, anxiety, and stress, and reporting in particular that her gastrointestinal symptoms had been ongoing the entire month. Ex. 2 at 8. He opined that Ms. Huelsenbeck's stomach issues were stress-related, and he prescribed an antacid medication and Celexa[7] for treatment. *Id.* Petitioner and Ms. Huelsenbeck speculated at one point that these GI symptoms may have been related to the Adderall prescription, as this group of symptoms had been noticed only after she began taking it. Ex. 20 at 322.

By mid-February, however, Ms. Huelsenbeck's headaches and GI-related symptoms became severe enough for her to be hospitalized at Windom Area Hospital in Windom, Minnesota. Ex. 4 at 20. The medical records from this hospitalization (occurring February 13 - 16, 2012) state that she reported her headaches had begun during the "summer of 2011." *Id.* They also (and for the first time in the relevant medical record) contained statements from Petitioner and/or Ms. Huelsenbeck suggesting a relationship to the HPV vaccine; thus, treaters were informed that Ms. Huelsenbeck had not experienced any reaction to the first HPV dose, but began experiencing "headache, nausea, vomiting" after her second HPV dose in August 2011. *Id.* These symptoms, she explained, had improved over time, but had returned after her third HPV vaccination and thereafter persisted. *Id.* The hospital treaters, by contrast, attributed her headaches to stress and anxiety, "most of which is related to school." *Id.*

During the February 2012 hospital stay, Ms. Huelsenbeck was treated with pain medication and Celebrex, and the treatments she received helped control her headaches, resulting in marked improvement. Ex. 4 at 21. She was ultimately discharged with a diagnosis of severe headaches, nausea, vomiting, dehydration, "migraine versus post HPV immunization," ADHD, anxiety, stress, and gastritis. *Id.* at 20. Her gastritis was attributed to high acid foods, and she was encouraged to take acid-reflux medication and to follow a low-acid diet. *Id.* at 21.

Not long after her discharge, Ms. Huelsenbeck returned to her PCP at the end of February, again complaining of the same set of headache/nausea symptoms that she had described in the

[7] Celexa is a trademark for citalopram hydrobromide. *Dorland's* at 312. Celexa is a serotonin reuptake inhibitor (SSRI) used to treat depression. *Citalopram (Oral Route)*, Mayo Clinic, https://www mayoclinic.org/drugs-supplements/citalopram-oral-route/description/drg-20062980 (last visited Oct. 23, 2017).

past. Ex. 2 at 6. The records from this visit memorialize the first time that any of her caregivers proposed that there might be some relationship between the HPV vaccine and her condition. Specifically, Dr. Hartberg stated that he was "wondering about the possibility of an irritation of the brain from her vaccination schedule, which seemed to correlate with onset of these headaches, nausea and vomiting." *Id.* As treatment, Dr. Hartberg prescribed a one-week course of oral steroids, which Ms. Huelsenbeck later identified as having helped reduce her headaches. *Id.* In response, Dr. Hartberg stated that "it makes me suspicious that her headaches are associated with the [HPV] vaccination, especially in terms of the correlation of the onset of headaches with the three injections of [HPV]." *Id*. at 6. However, he recommended that Ms. Huelsenbeck follow up with a neurologist to determine if anything else might explain her symptoms. *Id.*

Diagnosis of IIH

By the end of March 2012, Ms. Huelsenbeck began to experience blurry vision and diplopia,[8] and therefore sought treatment with Dr. Seth Consoer, an ophthalmologist. Ex. 7 at 4. Dr. Consoer assessed her with papilledema[9] and sixth or abducens nerve palsy, proposing that the diplopia was most likely attributable to a weakness of her sixth cranial nerve. *Id.* at 7. A brain MRI, however, ordered by Dr. Consoer, on March 27, 2012, revealed the existence of a probable pituitary microadenoma,[10] and thickening and enhancement of the tentorium cerebelli. *Id.* at 1.

On April 2, 2012, Ms. Huelsenbeck sought treatment from Dr. Vanessa Tseng, a neurologist at the Mayo Clinic, for further headaches relating to her diplopia. Ex. 3 at 60. At that time, Ms. Huelsenbeck recounted her history of headaches and recent onset of blurred vision. *Id.* The office visit notes made no mention of the HPV vaccine, however. *Id.* at 60-62. Dr. Tseng opined that Ms. Huelsenbeck might have a pseudotumor cerebri ("PC"), a neurological disorder equivalent to IIH, and ordered testing to confirm her hypothesis. *Id.* at 61.

The testing results were consistent with Dr. Tseng's suspicions. A lumbar puncture performed on April 2, 2012, revealed an elevated opening cerebral spinal fluid ("CSF") pressure of 47cm to 52cm. Ex. 3 at 32, 58. This CSF testing was otherwise negative for oligoclonal bands (thus reducing the likelihood that Ms. Huelsenbeck suffered from multiple sclerosis), and her IgG index and synthesis rate were also entirely normal. *Id.* at 56-58. After reviewing these results, Dr.

[8] Diplopia or double vision is defined as "the perception of two images of a single object." *Dorland's* at 525. Diplopia can take a variety of forms, including vertical, binocular, and crossed vision. *Id.*

[9] Papilledema is an edema of the optic disk (also referred to as a "choked disk"), resulting from increased intracranial pressure, malignant hypertension, or thrombosis of the central retinal vein. *Dorland's* at 1372.

[10] A microadenoma is a pituitary adenoma less than 10 mm in diameter. *Dorland's* at 1156.

Tseng assessed Ms. Huelsenbeck with PC and started her on Diamox and Lasix.[11] *Id.* at 62. Dr. Tseng did not opine or propose that the HPV vaccine was in any way related to Ms. Huelsenbeck's symptoms.

Two weeks into these PC-targeted treatments, Ms. Huelsenbeck reported that she was no longer having headaches, and Dr. Tseng noted that Ms. Huelsenbeck's left lateral rectus muscle seemed to be less stressed.[12] Ex. 3 at 42, 38. A repeat lumbar puncture now revealed that Ms. Huelsenbeck's CSF pressure was down to 23-24cm, which Dr. Tseng opined explained her improvement (as it evidenced a reduction in intracranial brain pressure). *Id.* at 39. By May 1, 2012, Ms. Huelsenbeck denied having experienced any recent headaches and reported that she felt generally well, leading Dr. Tseng to reduce her medication course somewhat. *Id.* at 32, 36.

Three months passed without incident or a recurrence of headaches before Ms. Huelsenbeck returned to the Mayo Clinic in September 2012. Ex. 3 at 22. She now reported that on August 30, 3012, she had experienced what she termed a "typical headache with pressure in the back of her head especially when she bends down to pick things up, or squatting," but without any associated vision problems. *Id.* In response, Dr. Tseng restarted Ms. Huelsenbeck on Lasix and also prescribed Topamax.[13] A repeat lumbar puncture, on September 18, 2012, however, revealed a normal spinal fluid opening pressure *Id.* at 14, 16.

Thereafter, on October 9, 2012, Petitioner brought Ms. Huelsenbeck to Dr. Zeenat Jaisani, a neurologist at Sanford Clinic Neurology, to obtain a second opinion. Ex. 6 at 3. At this time, Petitioner and Ms. Huelsenbeck provided a medical history that differed in significant detail from what prior treaters had been told. Thus, Ms. Huelsenbeck stated that her symptoms had started in June 2011, after her *first* HPV vaccination (contrary to her February statements that she had not experienced any reaction after the first dose), and that every time she received a subsequent vaccination, she had gotten worse. *Id.* at 5. She otherwise informed Dr. Jaisani that her headaches had recently returned in September 2012, but had resolved after a short course of steroids. *Id.* at 6.

[11] Diamox is used to treat PC by reducing cerebrospinal fluid, and Lasix is a diuretic used to reduce fluid in the body and increase urine output. *Pseudotumor cerebri*, Mayo Clinic, https://www.mayoclinic.org/diseases-conditions/pseudotumor-cerebri/diagnosis-treatment/drc-20354036 (last visited Oct. 24, 2017). Generally, physicians will start treatment with Diamox, then combine Diamox with Lasix if Diamox alone is not effective. *Id.*

[12] Dr. Tseng originally treated Ms. Huelsenbeck for a left lateral rectus palsy. Ex. 3 at 38. Sixth nerve palsy involves a nerve on the surface of the brain that controls eye movement. Tr. at 167. This nerve can be affected by pressure buildup resulting from a PC diagnosis. *Id.* Symptoms generally manifest as double vision. *Id.*

[13] *Id.* at 20. Topamax is a trademark for topiramate. *Dorland's* at 1939. It is used to treat migraine headaches and epilepsy. *Topiramate (Oral Route)*, Mayo Clinic, https://www.mayoclinic.org/drugs-supplements/topiramate-oral-route/description/drg-20067047 (last visited Oct. 24, 2017).

Dr. Jaisani diagnosed Ms. Huelsenbeck with PC, ADHD, anxiety, and depression, but did not propose that the HPV vaccines she had received could be causal. *Id.* at 4.

Later that fall, during a return visit to Dr. Jaisani in November 2012 prompted by new headaches, a repeat MRI was performed, producing normal results. Ex.6 at 26. This led Dr. Jaisani to propose that Ms. Huelsenbeck's anxiety might be causing her more recent symptoms rather than her previously-established PC, and prompting him to recommend that she begin treatment with a psychiatrist. *Id.* at 26-27. She subsequently received psychiatric care at the Mayo Clinic over the next six months. Ex. 3 at 1-2; Ex. 12 at 10, 77, 93. During a follow up with Dr. Jaisani on June 10, 2013, Ms. Huelsenbeck now reported that she had not suffered from a headache in the "longest time." Ex. 14 at 21.

The next year, on September 12, 2013, Ms. Huelsenbeck returned to Dr. Jaisani with complaints of headaches beginning in August of that year. Ex. 14 at 54. Dr. Jaisani noted, however, that her headaches had seemed to return only after she stopped taking Klonopin.[14] *Id.* A repeat lumbar puncture revealed normal CSF pressure. *Id.* at 115. Ms. Huelsenbeck was assessed with recurrent chronic headaches and prescribed specialized medication. *Id.* at 55. The records filed in this case for all subsequent periods thereafter deal almost exclusively with Ms. Huelsenbeck's psychiatric treatment rather than the headache-related symptoms at issue, and are thus not discussed (although they have been reviewed).

Testimony at Hearing

A. Petitioner's Witnesses

1. *Lynn Rolshoven*

Lynn Rolshoven is the Petitioner's sister and Ms. Huelsenbeck's aunt. She briefly testified at hearing about her observations of Ms. Huelsenbeck as a child. Tr. at 134. Ms. Rolshoven described Ms. Huelsenbeck as a caring, giving child, who was generally healthy. *Id.* Ms. Huelsenbeck was diagnosed with ADHD as a second grader, nearly twenty years ago. *Id.* at 134, 145. According to Ms. Rolshoven, Ms. Huelsenbeck also struggled with attention loss and an inability to sit still. *Id.* at 134. Further, Ms. Rolshoven testified, Ms. Huelsenbeck would fidget,

[14] Klonopin is a trademark for clonazepam. *Dorland's* at 989. Klonopin is a benzodiazepine, or central nervous system depressant, used to treat panic disorder and prevent seizures. *Clonazepam (Oral Route)*, Mayo Clinic, https://www.mayoclinic.org/drugs-supplements/clonazepam-oral-route/description/drg-20072102 (last visited Oct. 24, 2017).

and forget to turn in her homework assignments. *Id.* at 135. However, she was able to participate in athletics and music classes. *Id.*

Ms. Rolshoven accompanied Ms. Huelsenbeck on the day she received her second HPV vaccine in August 2011. Tr. at 136. According to Ms. Rolshoven, Ms. Huelsenbeck did not experience any adverse reaction to the vaccine on that day. *Id.* Consistent with Petitioner's statements made to Dr. Jaisani, Ms. Rolshoven testified, Ms. Huelsenbeck first experienced a severe headache at a church event in September 2011, and then again during Christmas of that year. *Id.* at 137-38. In addition, Ms. Huelsenbeck began to experience debilitating vomiting during Thanksgiving, and double vision around New Year's Day. *Id.* at 140. According to Ms. Rolshoven, the headaches were initially mild but grew increasingly intense, resulting in debilitating pain. *Id.* at 136. Ms. Rolshoven further testified that Ms. Huelsenbeck would routinely "lay in bed or lay on the couch, in a dark room" and cry constantly due to the pain. *Id.*

Ms. Rolshoven expressed frustration that treaters could not explain Ms. Huelsenbeck's headache condition, noting that Ms. Huelsenbeck remained in intense pain throughout most of the fall of 2011 and had repeatedly missed school as a result. Tr. at 138. Ms. Rolshoven further testified to her continued concern for Ms. Huelsenbeck, noting that she has struggled with behavioral problems in the past and continues to suffer from memory problems. However, Ms. Huelsenbeck is currently able to care for herself and her children on a daily basis. *Id.* at 141-42. Despite the above, Ms. Huelsenbeck cannot maintain a job, and is at present unemployed. *Id.* at 143.

2. *Dr. Lawrence Steinman*

Petitioner's expert, Dr. Steinman, filed two written reports in this case, and testified at hearing. *See* Expert Report, dated Aug. 4, 2015, filed as Ex. 25 (ECF No. 24) ("Steinman First Rep."); Expert Report, dated Mar. 26, 2016, filed as Ex. 26 (ECF No. 30-1) ('Steinman Second Rep."). According to Dr. Steinman, Ms. Huelsenbeck's headache condition and subsequent sequelae were a direct result of receipt of the HPV vaccine.

Dr. Steinman is a professor in Stanford University's Departments of Neurology, Pediatrics, and Genetics, and the chair of Stanford's Immunology Program. Steinman First Rep. at 2-3. He has been elected to the Institute of Medicine ("IOM") in neurology, and he has published extensively, including articles related to his research on autoimmune diseases and molecular mimicry. *Id.* at 2. He is also board certified by the American Board of Psychiatry and Neurology. *Id.* at 3. Dr. Steinman's report indicated that he has treated over 1,000 patients with headaches spanning his 35 year career with Stanford Children's Hospital, including adult and pediatric neurology patients. *Id.*

Dr. Steinman testified at hearing that he regularly sees 10 to 20 patients per month, as either consults or inpatients. Tr. at 12. While Dr. Steinman treats patients for a wide variety of neurologic disorders, headaches are the most common disorder he has treated over the course of his career. *Id.* at 11. Further, Dr. Steinman stated that he has diagnosed roughly 100 patients with IIH or PC. *Id.* at 11-12.

Dr. Steinman maintained that the HPV vaccine caused Ms. Huelsenbeck's chronic headaches and psychological sequelae resulting from her PC diagnosis. Steinman First Rep. at 1. Dr. Steinman defined PC as a headache condition caused by increased pressure in the brain. Tr. at 31. According to Dr. Steinman, Ms. Huelsenbeck began to experience a variety of headaches, including (but not limited to) PC-related headaches, following her second HPV vaccination, which resolved after treatment but returned after her third HPV vaccination. *Id.* at 27, 57. In Dr. Steinman's view, Ms. Huelsenbeck's IIH/PC diagnosis was not the complete cause of her headaches, however; the HPV vaccine explained *some* of the headaches. Tr. at 33-34. His theory therefore differentiated between headaches attributable solely to her diagnosed PC and those purportedly caused by the HPV vaccine. *Id.* at 20. Dr. Steinman argued that differences between the sources of Ms. Huelsenbeck's headaches, although subtle, could be discerned in her chronologic medical history; thus, he noted that even after Ms. Huelsenbeck's IIH/PC was successfully treated, and her intracranial pressure was controlled, she continued to experience headaches, allowing for the possibility that such subsequent headaches might not be attributable to PC. *Id.* at 17-18, 32, 73.[15]

At hearing, Dr. Steinman characterized Ms. Huelsenbeck's injury as "headaches." Tr. at 11, 14. Headaches do not occur or originate within the brain itself, but in the "head" – specifically, the structures surrounding the brain. *Id.* at 16. For the HPV vaccine to trigger headaches, Dr. Steinman proposed, the "immune system need only advance as far as the blood vessels, without the need to enter the brain, where demyelination might be triggered." Steinman Second Rep. at 2. As a result, the absence in this case of evidence of a central nervous system inflammatory process producing demyelination (for example, tests revealing the presence of demyelinating antibodies, such as oligoclonal bands, or other indicia of generalized inflammation) did not in his view undermine his theory. Tr. at 61-62, 64, 67, 97. Indeed, Dr. Steinman made clear that his theory did *not* rely on the existence of a demyelinating process involving nerve damage. *Id.* at 15-16, 62, 64; Steinman Second Rep. at 1 ("I do NOT contend that demyelination is at all necessary [in this case]").

[15] On cross examination, Dr. Steinman was confronted with the fact (as set forth in the factual summary above) that Ms. Huelsenbeck was successfully treated for IIH/PC, leading to a months-long cessation of her headaches before she began to experience them again. Tr. 101-02; Ex. 3 at 36. In response, Dr. Steinman (proposing that "there is no hard and fast definition" for reoccurrence) maintained that the reoccurrence in this case was likely caused by an autoimmune process, even though he could not fully explain why. *Id.* at 105, 103-04.

According to Dr. Steinman, the HPV vaccine triggered Ms. Huelsenbeck's headache condition via the mechanistic process of molecular mimicry. Steinman First Rep. at 1. Dr. Steinman has generally proposed a concept that has been largely accepted in the medical community, and often in the Vaccine Program as well (albeit not with respect to the specific theory alleged in this case): that antibodies (whether induced by a vaccine or infectious agent) can mistakenly cross-react with myelin basic protein ("MBP") (a primary protein component of human nerves), causing damage to a nerve's myelin sheath and resulting in disease. *Id.* at 1, 8-14; *see* L. Steinman, *Autoimmune Disease*, Scientific American 107 (1993), filed as Ex. 27 (ECF No. 51-1) ("Steinman"); Steinman First Rep. at 1. While Dr. Steinman acknowledged that his overarching theories about autoimmune cross-reactive processes involving MBP usually pertain to central nervous system structures and illnesses (something he had already ruled out as relevant in this case), he maintained that because (as discussed below) the outer blood-brain barrier structures also contain MBP, his theory "works" in this case as well. Tr. at 64.

Dr. Steinman opined that the molecular mimicry theory applicable to this case consists of two main mechanisms, both involving alum - an adjuvant added to the HPV vaccine to elicit a stronger immune response. Tr. at 42. First, alum activates an inflammasome,[16] which in turn triggers the production of cytokines.[17] *Id.* at 41; Steinman First Rep. at 28-31; L. Chen, et al., *Chemical Stimulation of the Intracranial Dura Activates NALP3 Inflammasome in Trigeminal Ganglia Neurons*, 1566 Brain Research 1 (2014), filed as Ex. 52 (ECF No. 52-3). Headaches result when those cytokines stimulate the trigeminal ganglion, a sensory ganglion of the trigeminal nerve that innervates the face and serves as a processing center for pain responses. Tr. at 42.

Second, Dr. Steinman opined that the alum component of the HPV vaccine encourages an immunological cross-reaction between peptide components of the HPV vaccine and the MBP found in cerebral blood vessels, much as his theory has proposed a reaction between antibodies produced in response to a vaccine and MBP in nerve structures. Tr. at 29-30, 37. Thus, an inflammatory response at the blood-brain barrier interferes with the reabsorption of spinal fluid, and the increased spinal fluid, in turn, results in the heightened CSF pressure characteristic of IIH (although Dr. Steinman later admitted an absence of evidence of inflammation). *Id.* at 52, 55, 129. Taken together, Dr. Steinman asserted that the alum component triggers cytokine production (causing pain), while also enhancing the cross-reaction with the MBP also found in cerebral blood

[16] "Inflammasome" is a term used to describe a complex system of proteins found in phagocytic cells. *Dorland's* at 936. Inflammasomes are necessary for the activation of cytokines during an inflammatory response. *Id.*

[17] Cytokine is a term for nonantibody proteins that act as intercellular mediators during an immune response. *Dorland's* at 466.

vessels, inhibiting the reabsorption of cerebral spinal fluid and resulting in headaches. *Id.* at 42, 55.[18]

In support of his molecular mimicry theory, Dr. Steinman relied on a number of items of medical literature detailing how antibodies can cross-react with MBP, albeit in different contexts and/or involving different diseases. *See, e.g.,* Steinman First Rep. at 10-13, 33-35; K. Wucherpfennig, et al., *Structure of Human T-cell Receptors Specific for an Immunodominant Myelin Basic Protein Peptide: Positive of T-cell Receptors on HLA-DR2/Peptide Complexes*, 92 Proc. Natl. Acad. Sci. 8896 (1995), filed as Ex. 35 (ECF No. 51-9) ("Wucherpfennig") (studying the interplay between antigenic peptides and T-cell receptors); S. Haussmann, et al., *Structural Features of Autoreactive TRC That Determine the Degree of Degeneracy in Peptide Recognition*, 162 J. Immunology 338 (1999), filed as Ex. 34 (ECF No. 51-8); A. Gautam, et al., *A Polyalanine Peptide with Only Five Native Myelin Basic Protein Residues Induces Autoimmune Encephalomyelitis*, 176 J. Exp. Med. 605 (1992), filed as Ex. 40 (ECF No. 43-4). But these articles largely involved contexts in which MBP was either understood or reasonably suspected to be the relevant target antigen central to an autoimmune process relating to a neuropathic illness of some kind. *See, e.g.,* Wucherpfennig at 8896 (noting that studies had already shown MBP peptide sequences involved in theorized autoimmune cross-reaction were "associated with susceptibility to multiple sclerosis"). None of these items of literature, however, stand for the proposition that MBP located in blood vessel structures near the brain is associated with a disease process resulting in the kind of headaches complained of in this action, and Dr. Steinman admitted he had no direct experience studying MBP cross-reactivity at this location in the body. Tr. at 127.

To connect his general theory about autoimmunity impacting MBP in the central nervous system with the present circumstances, Dr. Steinman relied primarily on a study that he maintained supported his opinion that MBP is in fact found also in the blood vessels surrounding the brain. J. Li, et al., *Rat Blood-Brain Barrier Genomics II*, 22 J. Cerebral Blood Flow & Metabolism 1319 (2002), filed as Ex. No. 60 (ECF No. 54-1) ("Li"); Steinman First Rep. at 13. The Li study involved profiling genes differentially expressed in the microvasculature of a rat brain that "provides the interface between blood and brain." Li at 1319. Li determined that approximately half of the genes identified had a known function, and half were either rat-expressed sequence tags, or novel genes. *Id.* Among other things, the study concluded that a gene responsible for expression of MBP is found in the rat brain microvasculature. *Id.* at 1323. Li suggests that "immune reactions against myelin-related proteins, such as myelin basic protein . . . ., may originate at the brain microvasculature, where these myelin-related proteins are also expressed." *Id.* But Li did not test this speculative comment, and supported it with other literature involving demyelinating

[18] Dr. Steinman's expert report went on to provide a detailed explanation of possible mimics between protein sequences contained in components of the HPV vaccine and the MBP. *See generally* Steinman First Report at 8-18.

conditions – which Dr. Steinman concedes are *not* at issue in causing Ms. Huelsenbeck's headaches. *Id.* (citations omitted).

One item of literature cited by Dr. Steinman as possibly establishing a more direct link between the HPV vaccine and vasculitis or similar headache-causing conditions prompted heated questioning by Respondent. *See* L. Tomljenovic, et al., *Death after Quadrivalent Human Papillomavirus (HPV) Vaccination: Causal or Coincidental?* 12 Pharmaceut. Reg. Affairs 1-11 (2012), filed as Ex. 29 (ECF No. 51-3) ("Tomljenovic"). Tomljenovic involved post-mortem brain tissue analyses of two young women, ages 14 and 19, who had experienced cerebral vasculitis-type symptoms following the HPV vaccination. Tomljenovic at 1. In case one, a 19-year-old female died in her sleep six months after receipt of an HPV vaccine, exhibiting symptoms before death such as fatigue, muscle weakness, tachycardia, chest pain, tingling, irritability, and mental confusion. *Id.* at 2. In case two, a 14-year-old female died 15 days post-vaccination, and exhibited symptoms including more severe migraines, speech problems, dizziness, weakness, inability to walk, depressed consciousness, and vomiting, all of which gradually resolved up until her death. *Id.*

In both cases, autopsy reports were inconclusive. Tomljenovic at 2. Upon reviewing brain tissue specimens, Tomljenovic found clear evidence of the presence of HPV-16L1 particles attached to the blood vessel wall within the cerebral vasculature, concluding from this that an autoimmune vasculitis could be triggered by cross-reactive HPV-16L1 antibodies binding to the cerebral blood vessel wall. *Id.* at 3. Dr. Steinman cited Tomljenovic in his first report as support for his theory that structures within blood vessels near the brain could cross-react with components of the HPV vaccine. Steinman First Rep. at 12.

Respondent's expert, however, called the validity of Tomljenovic into question, identifying a Centers for Disease Control and Prevention ("CDC") "Technical Report" issued by the CDC's Clinical Immunization Safety Assessment working group (comprised of researchers from several nationally-recognized academic institutions with particularized medical expertise, like Johns Hopkins and Duke Universities) that expressly criticized Tomljenovic's findings for poor methodologies and other errors. *See* CDC, *Technical Report: Review of a Published Report of Cerebral Vasculitis after Vaccination with the Human Papillomavirus (HPV) Vaccine* 1-4 (2012), filed as Ex. 58 (ECF No. 52-9) (the "CDC Technical Report"); *see also* CDC, *Clinical Immunization Safety Assessment (CISA) Project* 1-3 (2015), filed as Ex. 59 (ECF No. 52-10). In response, Dr. Steinman attacked the anonymity of the CDC Technical Report's authors, which he maintained made it impossible to assess the validity of their critiques. Tr. at 81-82.[19] However, Dr.

[19] Dr. Steinman overstated the significance of the anonymity of the CDC Technical Report's authorship. At first, he asserted that the CDC Technical Report was only one of 42 similar "technical" reports in which the authors were not identified, thereby highlighting the suspiciousness of its failure to disclose its authors. Yet on cross examination, he

Steinman repeatedly evaded answering questions about the specific critiques that were leveled at Tomljenovic by the CDC Technical Report, including the assertions that (a) no clearly presented evidence had established that the studied patients had been diagnosed with histologic vasculitis, (b) the study lacked sufficient controls, and (c) the study failed to utilize the proper equipment in analyzing tissue samples. *Id.* at 84-86, 87 (agreeing that he "didn't see evidence" of test results cited in Tomljenovic that would support vasculitis diagnosis), 91-94. Ultimately, Dr. Steinman acknowledged that Tomljenovic was not instrumental to his overall causation theory. *Id.* at 114 ("I was ready to reject that paper").

Other than Tomljenovic, Dr. Steinman identified nothing in the way of supporting scientific or medical literature linking the HPV vaccine to Ms. Huelsenbeck's symptoms or condition, whether directly diagnosed (PC/IIH) or implied (vasculitis) in his initial report. *See, e.g.*, Tr. at 71-72 (no literature linking vasculitis and PC, and admitting PC is not known to be autoimmune in character), 76 ("[t]his is the theory to explain why Gardasil in this specific case causes headache, which is well known, and *I don't think anywhere in the scientific literature you're going to find an article*, because I certainly can't find it, that gets into the mechanistic understanding of the fact")(emphasis added), and 107 (admitting no case studies involving HPV and headaches). He did, however, maintain that the vaccine's package inserts identified headache as a known (if immediate) post-vaccine reaction, thus providing reliable evidence that supported his opinion. *Id.* at 14-15, 17. He also noted that early clinical trials of Gardasil run by the Food and Drug Administration had corroborated this, even though the alleged chronic headaches that he maintained had been discerned through such trials had not been included in the package insert warnings, for reasons he could not explain. *Id.* at 45, 47-48, 107. And he proposed that evidence about the long-lasting antibody response to the HPV vaccine also was consistent with the chronic nature of Ms. Huelsenbeck's headaches. *Id.* at 59-60.

In addition, Dr. Steinman relied on a postlicensing study detailing all adverse events reported to have followed HPV vaccination. *See* B. Slade, et al., *Postlicensure Safety Surveillance for Quadrivalent Human Papillomavirus Recombinant Vaccine*, 302 JAMA 750, 750 (2009), filed as Ex. 32 (ECF No. 51-6) ("Slade"). The intended purpose of Slade was to summarize all post-HPV vaccine events reported to VAERS[20] between June 2006 and December 2008. *Id.* Dr. Steinman referred to the Slade paper specifically, noting that headaches were a common complaint following HPV vaccination ("[t]here were 937 reports of headaches after qHPV vaccination") –

agreed that in fact the other CDC reports to which he compared it had been formally published, making them distinguishable. *See* Tr. at 83 ("[s]o, technically, I was lumping them all together").

[20] The Vaccine Adverse Event Reporting System ("VAERS") is a national warning system designed to detect safety problems in U.S.-licensed vaccines. *See About VAERS*, VAERS, https://vaers.hhs.gov/about.html (last visited Jan. 10, 2018). It is managed by both the CDC and the FDA. VAERS monitors and analyzes reports of vaccine related injuries and side effects from both healthcare professionals and individuals.

although Slade also placed that number in context, adding that such headache complaints comprised only 7.7 percent of the total events reported. *Id.* at 753.

As to onset, Dr. Steinman opined that (consistent with the medical record) Ms. Huelsenbeck's symptoms commenced about two weeks after the second HPV vaccine administration (although his first expert report seemed to mistakenly identify the first dose as the start of her symptoms). *Compare* Steinman First Rep. at 2 *with* Tr. at 17. According to Dr. Steinman, two weeks was an "optimal" timeframe for the occurrence of an immunologic response, making a ten-day onset temporally appropriate for an adverse reaction. *Id.* at 57. Dr. Steinman agreed, however, that symptoms occurring too soon (within a day of vaccination) or too long (eight weeks later) after vaccination would not be medically appropriate. *Id.* at 58.

To support the onset/timing component of his opinion, Dr. Steinman relied on the Schoenberger and Langmuir studies. Steinman First Rep. at 32; *see* L. Schoenberger, et al., *Guillain-Barre Syndrome Following Vaccination in the National Influenza Immunization Program, United States, 1976-1977*, 110 Am. J. Epidemiology 105 (1979), filed as Ex. 53 (ECF No. 52-4); A. Langmuir, et al., *An Epidemiological and Clinical Evaluation of Guillain-Barre Syndrome Reported in Association with the Administration of Swine Influenza Vaccine*, 119 Am. J. Epidemiology 841 (1984), filed as Ex. 54 (ECF No. 52-5). Taken together, these two studies concluded that a medically appropriate timeframe for onset of Guillain-Barré syndrome ("GBS") (a peripheral neuropathy mediated by an autoimmune process resulting in demyelination) following the flu vaccine is five to six weeks at the least. However, Dr. Steinman acknowledged that it is "unclear" if it is scientifically reasonable to substitute swine flu and GBS for HPV and headaches. Steinman First Rep. at 32. Dr. Steinman also specifically acknowledged that, unlike GBS (which has been the subject of extensive medical and scientific study linking vaccination to it), no epidemiological studies have been conducted linking the HPV vaccine to headaches of the kind his theory proposed occurred in this case. *Id.*

Dr. Steinman struggled to minimize Ms. Huelsenbeck's IIH diagnosis as the best explanation for her symptoms. Dr. Steinman maintained that IIH can involve a vascular component, yet at the same time acknowledged that Ms. Huelsenbeck's MRI showed no evidence of vasculitis. Tr. at 38, 72. Indeed, he insisted he was *not* opining that she had vasculitis, as Respondent's expert initially interpreted his opinion to hold. *Id.* at 258-59. Dr. Steinman also dismissed, but did not rebut, the contention by Respondent that vasculitis is generally detected 90 percent of the time in PC/IIH cases, arguing that Ms. Huelsenbeck was prescribed a steroidal medication, Prednisone, at the time of her MRI, which could explain the absence of vasculitis evidence in her MRI (despite the sensitivity of imaging in this regard). *Id.* at 77-78, 97, 123. Thus, according to Dr. Steinman, Ms. Huelsenbeck's MRIs did not alter his theory in the present case.

Id. He otherwise insisted that components of the HPV vaccine could cross-react with MBP and cause headaches without resulting in vasculitis. *Id.* at 259, 261.

Throughout his testimony, Dr. Steinman made numerous statements revealing his personal conception of the tasks of a Vaccine Program expert (while also suggesting he did not have complete confidence in his theory's reliability). Thus, Dr. Steinman admitted that his causation theory in this case was not "100 percent certain, by any means" (Tr. at 51), although he nevertheless proposed that (given that an expert's "task is to make a theory" (*Id.* at 64)), it was sufficient to meet the Program's preponderance evidentiary test. He even admitted that his opinion in this case was a "step beyond" his usual area of expertise, but maintained that his responsibility as an expert to offer a supporting causation theory overrode such concerns. Tr. at 126, 64.

In particular, to explain his duty as an expert, Dr. Steinman employed the metaphor of a "river" that he must cross "stone to stone":

> So I'm doing this step by step by step to get across a river. I'm putting together one piece of science with another piece of science to try to explain in part in this case how a disease named idiopathic could be caused by a vaccine.

Tr. at 21. In so stating, however, Dr. Steinman implicitly admitted that his efforts in this case had not been fully successful. *Id.* at 19 ("in some areas I can make a stronger and more compelling theory than others"). And he also admitted the widely-accepted medical view that the etiology of IIH was mostly understood to be unknown, despite the opinion offered in this action. *Id.* at 39 ("in the face of a disease called idiopathic, the best I can do, with all of the limitations, is go to the literature and construct a theory").

B. Respondent's Expert – Dr. Michael Kruer

Dr. Kruer submitted two written reports in this case, and testified at hearing. *See* Expert Report, dated January 15, 2016, filed as Ex. A (ECF No. 26-1) ("Kruer First Rep."); Expert Report dated July 31, 2016, filed as Ex. C (ECF No. 38-1) ("Kruer Second Rep."). Dr. Kruer is an adult and pediatric neuroimmunologist, and currently serves as an associate professor of child health, genetics, neurology, and molecular and cellular medicine at the University of Arizona College of Medicine. Tr. at 157. He is board certified in neurology, with special qualifications in pediatric neurology and neurodevelopmental disabilities. *See* Ex. B (Kruer CV) at 1; Tr. at 156. Dr. Kruer received his medical degree from the University of Arizona College of Medicine in Tucson. Ex. B at 3. He completed his residency in pediatrics at Phoenix Children's Hospital and a post-doctoral

fellowship in molecular neurogenetics at Oregon Health & Sciences University. *Id.* Dr. Kruer maintains his medical license in the State of Arizona. *Id.*

In his clinical practice, Dr. Kruer regularly sees patients several times a week. Tr. at 155. He cares for adults and children with immune-mediated neurological diseases. Ex. A at 1; Tr. at 156-57. In his research practice, he has identified new diseases and discovered novel autoantibodies involved in neurologic diseases. At hearing, Dr. Kruer testified that his research focus is neurogenetics and neuroimmunology, with an interest in characterizing autoantibody causes of neurological disease, specifically cerebral palsy, although only ten percent of his research efforts focus on autoimmune conditions. Tr. at 160; 242. Dr. Kruer has diagnosed and treated children with headaches, PC/IIH, and cerebral vasculitis. Ex. A at 1; Tr. at 157. In particular, he has treated a "couple dozen" patients with PC. Tr. at 157.

At hearing, Dr. Kruer attributed Ms. Huelsenbeck's symptoms to her underlying IIH diagnosis rather than receipt of the HPV vaccine. Tr. at 163,168; Kruer First Rep. at 10-11. Similar to Dr. Steinman, Dr. Kruer defined PC/IIH as an "elevation of pressure within the head" and noted that it is generally more prevalent in women and overweight individuals. *Id.* at 163. Symptoms include a lack of alternate imaging explanation and elevated intracranial pressure, and PC/IIH is typically diagnosed using a cerebral spinal fluid exam. *Id.* at 164-65. The headaches associated with IIH, according to Dr. Kruer, manifest as a direct result of increased intracranial pressure. *Id.* at 166. They are thus distinct from transient, self-limiting headaches not similarly attributable to CSF pressure levels. Kruer Second Rep. at 3; D. Friedman, et al., *Revised Diagnostic Criteria for the Pseudotumor Cerebri Syndrome in Adults and Children*, 81 Neurology 1159, 1162 (2013), filed as Ex. A, Tab 7 (ECF No. 27-7).

Dr. Kruer agreed with Ms. Huelsenbeck's IIH diagnosis, given the increased pressure levels in her CSF as determined by Dr. Tseng's testing. Tr. at 188, 234. In addition, Dr. Kruer agreed with the medical treatment prescribed by Dr. Tseng following the diagnosis, including Diamox, Acetazolamide, and Prednisone, and noted that this medication regimen resulted in the resolution of Ms. Huelsenbeck's headaches by April 2012. *Id.* at 189-90. Dr. Kruer acknowledged that Ms. Huelsenbeck experienced a reoccurrence of headaches several months later, and that it was difficult to know why, but proposed that the reoccurrence could have been caused by discontinuance of certain medications (in particular, birth control[21]), anxiety, pregnancy, or a general familial history. *Id.* at 180, 193, 245. Those same records, however, in Dr. Kruer's opinion established that the most likely source of Ms. Huelsenbeck's symptoms after the second HPV dose was IIH or PC. *Id.* at 167-68.

[21] On cross examination, however, Dr. Kruer acknowledged that the record did not allow him to conclusively determine when Ms. Huelsenbeck was in fact taking birth control. Tr. at 246-48.

Dr. Kruer dismissed Dr. Steinman's contention that the HPV vaccine might explain headaches that Ms. Huelsenbeck experienced after her successful IIH treatment. Kruer Second Rep. at 3. Although he acknowledged that minor, transient headaches could occur post-vaccination, in his understanding the existing medical literature did not support a relationship between vaccines and IIH. *Id*. He also questioned the reliability of Dr. Steinman's theory that alum could induce cytokine expression sufficient to cause chronic headaches. Tr. at 211. Although Dr. Kruer acknowledged that a cytokine response can cause fever, he contended that cytokines observed in post-vaccination fever *over a month later* could not be reasonably understood as having the capacity to induce headaches. *Id.* at 238, 251. And he dismissed VAERS-based literature presented by Dr. Steinman showing an increased instance of headaches following the HPV vaccine, arguing that none of the articles addressed increased incidence of IIH following HPV vaccination. *See e.g.*, B. Slade, et al., *Postlicensure Safety Surveillance for Quadrivalent Human Papillomavirus Recombinant Vaccine*, 302 JAMA 750, 753 (2009), filed as Ex. C, Tab 2 (ECF No.38-3). Otherwise, Dr. Kruer maintained that no reliable scientific evidence supported Petitioner's contention that vaccinations can cause PC/IIH, or that the HPV vaccine can induce injury to the blood vessels on the blood-brain barrier. Kruer First Rep. at 11; Tr. at 211.

Besides challenging the general association between the HPV vaccine and Ms. Huelsenbeck's headaches, Dr. Kruer also questioned the element of Dr. Steinman's theory positing molecular mimicry as the applicable biologic mechanism. Kruer First Rep. at 4. Dr. Kruer opined that the sequence homology presented by Dr. Steinman was not significant enough to warrant a conclusion that molecular mimicry could have caused Ms. Huelsenbeck's symptoms because protein homology, or amino acid residue, is common to all proteins generally. Tr. at 201.[22] Virtually every viral antigen will have some degree of sequence homology with protein sequences found throughout the human body. *Id.* at 201-02; Kruer First Rep. at 5. Thus, the presence of MBP in vascular structures like blood vessels does not mean that cross-reactivity involving MBP in other contexts also applies herein, and no evidence was offered to establish otherwise. Tr. at 207, 229; Kruer Second Rep. at 2.

Dr. Kruer also pointed out that the medical record did not bulwark Dr. Steinman's proposal that molecular mimicry had even occurred, since there was no corroborating evidence of an ongoing autoimmune process. Kruer First Rep. at 6, 9-10; Kruer Second Rep. at 4; Tr. at 167, 188.

[22] Dr. Kruer also opined that the literature referenced by Dr. Steinman to establish autoimmune cross-reactivity with MBP relied on studies that were designed specifically to produce that outcome, based on selected peptide sequences designed to induce autoreactivity, augmented with a specific type of strong adjuvant (Freund's adjuvant) that is not used in human vaccines. Tr. at 204-07; S. Bittner, et al., *Myelin Oligodendrocyte Glycoprotein (MOG35-55) Induced Experimental Autoimmune Encephalomyelitis (EAE) in C57BL/6 Mice*, 86 J. Vis. Exp. E51275 (2014), filed as Ex. A, Tab 3 (ECF No. 27-3); L. Markowitz, et al., *Quadrivalent Human Papillomavirus Vaccine: Recommendations of the Advisory Committee on Immunization Practices (ACIP)*, CDC, filed as Ex. A, Tab 8 (ECF No. 27-8).

For example, testing identified no oligoclonal bands in the CSF, the presence of which would reveal autoimmune activity within the central nervous system. Kruer First Rep. at 6-7; A. Sinclair, et al., *Clinical Association of Intrathecal and Mirrored Oligoclonal Bands in Pediatric Neurology*, 55 Developmental Med. & Child Neurology 71, 72 (2013), filed as Ex. A, Tab 11 (ECF No. 27-11). There was also no monoclonal gammopathy on the serum protein electrophoresis, which would detect autoimmune-associated antibodies, and Ms. Huelsenbeck's antibody production was otherwise normal. Kruer First Rep. at 6-7.

In addition to addressing the opinion Dr. Steinman seemed to favor at hearing, Dr. Kruer also addressed the opinion he understood Dr. Steinman to set forth in his first report: that Ms. Huelsenbeck's headaches could be attributed to cerebral vasculitis. Tr. at 170, 183; Kruer First Rep. at 8; Kruer Second Rep. at 3. Dr. Kruer defined vasculitis as a rare, severe neurological condition characterized by inflammation of blood vessels within the brain. Tr. at 170. Vasculitis is diagnosed based on three principal criteria, including a history of unexplained neurological deficiencies; some form of vascular inflammation in the angiography or histopathology in the central nervous system; and no evidence of systematic vasculitis or other medical condition that could explain the symptoms. *Id.* at 170-71; Kruer First Rep. at 9; L. Calabrese & J. Mallek, *Primary Angiitis of the Central Nervous System*, 67 Medicine 20, 20 (1987), filed as Ex. A, Tab 5 (ECF No. 27-5). The primary neuroradiographic modality used to diagnose vasculitis is the MRI. *Id.* at 172; *see also* A. Rodriguez, et al., *Primary Angiitis of the Central Nervous System in Adults and Children*, 41 Rheum. Dis. Clin. N. Am. 47 (2015), filed as Ex. A-10 (ECF No. 27-10).

Those diagnostic criteria were not met based on Ms. Huelsenbeck's record. Tr. at 170. If vasculitis had been present, a treater would have seen "hyperintense or bright FLAIR or T-2 lesions" or edema injury on the MRI – but Ms. Huelsenbeck's MRI showed nothing of the sort (although it was consistent with an IIH diagnosis). *Id.* at 184, 186; Kruer First Rep. at 9. In addition, testing indicated no evidence of elevated protein levels within the central nervous system, and no oligoclonal band formation, both of which would be expected. *Id.* at 186. Dr. Kruer further opined that untreated vasculitis generally takes a progressive course, resulting in more severe symptoms over time, but that was inconsistent with Ms. Huelsenbeck's presentation. *Id.* at 194.

Dr. Kruer dismissed the Tomljenovic article partially relied on by Dr. Steinman to support the contention that the HPV vaccine can cause cerebral vasculitis. Kruer First Rep. at 5-6; Kruer Second Rep. at 2-3 As Dr. Kruer argued, Tomljenovic "flagrantly mispresent[ed]" certain facts about its findings, presented no clear evidence that the study's subjects had been diagnosed with histologic vasculitis, and made errors in its methodology. *Id.* at 212; Kruer First Rep. at 5-6. In addition, he referenced the CDC Technical Report, which had determined that Tomljenovic misinterpreted histopathology and immunopathology methods used in the study when concluding that the HPV vaccine might be causally related to autoimmune cerebral vasculitis. Kruer Second

Rep. at 1; Kruer First Rep. at 5-6; CDC Technical Report at 2-3. Dr. Kruer therefore deemed Tomljenovic unreliable support for any relationship proposed between the HPV vaccine and vasculitis. Kruer First Rep. at 6.

In addition to highlighting the lack of literature support for a link between HPV and vasculitis, Dr. Kruer reviewed Ms. Huelsenbeck's medical history in an effort to demonstrate that she could not be deemed to have suffered from it. Dr. Kruer acknowledged that headaches are a symptom of vasculitis, but maintained that vasculitis would be accompanied by more severe symptoms, like brain damage manifesting with motor control or ataxia problems. Tr. at 176. Simply having chronic or reoccurring headaches would not satisfy the diagnostic requirements for vasculitis, even over a ten-month period. *Id.* at 175. Dr. Kruer acknowledged that headaches associated with vasculitis could be intermittent, but noted that vasculitis is an "aggressive and progressive" condition that often results in severe disability, or even death. *Id.* at 177. Given her medical record, Ms. Huelsenbeck's treating physician never diagnosed her with vasculitis. *Id.*

Dr. Kruer also reviewed the treatments Ms. Huelsenbeck received, in response to Dr. Steinman's suggestion that certain medications (in particular, steroids) might have either revealed, or masked, the true nature of her condition. In his experience, vasculitis treatment typically includes aggressive cytotoxic agents, or cyclophosphamide - a chemotherapeutic agent used to treat cancer. Tr. at 175. Prednisone is also used to treat vasculitis at onset, but is not sufficient to "push th[e] condition into remission." *Id.* In Ms. Huelsenbeck's circumstances, the "bursts" of Prednisone in the amounts she received would not have been effective if vasculitis were the proper diagnosis, but were appropriate for IIH/PC. *Id.* at 176, 254-55. Rather, according to Dr. Kruer, effective treatment of vasculitis would require 20 times the dosage of steroid administered to Ms. Huelsenbeck. *Id.* at 255.[23] Dr. Kruer also dismissed Dr. Steinman's argument that Prednisone could have masked the existence of vasculitis on Ms. Huelsenbeck's MRI, given the low dosage she was receiving. *Id.* at 198-99.

On cross examination, Dr. Kruer acknowledged some limitations to his opinion. He agreed that a variety of conditions can produce headaches, and that they can occur without the kind of severe brain injury he proposed was consistent with vasculitis. Tr. at 217-20. He admitted that Ms. Huelsenbeck *did* experience headaches after her IIH/PC had resolved, and that he could not explain their cause. *Id.* at 222-23. He also agreed that sound medical literature supports the conclusion that

[23] By contrast, the "first line" of treatment for IIH/PC is not steroids but specific medications (Acetazolamide or Diamox) used to decrease CSF production. Tr. at 165, 169. Prednisone and corticosteroids are nevertheless used as a "second line" treatment for PC/IIH – particularly when eyesight is threatened by the excess pressure - and therefore (in Dr. Kruer's opinion) the administration of steroids in this case did not support the alternative etiology for her headaches proposed by Dr. Steinman. *Id.* at 166, 195-96, 252; F. Distelmaier, et al., *Pseudotumor Cerebri as an Important Differential Diagnosis of Papilledema in Children*, 28 Elsevier 190, 192-93 (2008), filed as Ex. H (ECF No. 56-3).

cytokine levels have been measured to increase after a post-vaccination fever, although he resisted concluding from this that there was a causal relationship between fever and vaccine-induced cytokines. *Id.* at 238-39. In the same vein, Dr. Kruer was asked about whether Ms. Huelsenbeck might have been running a fever after her third HPV dose (thus allowing for the possible inference that cytokine upregulation consistent with Dr. Steinman's theory had occurred and produced her next round of headaches). In response, Dr. Kruer disputed how high her fever was, and posited that it could not otherwise be causally linked to a resumption of headaches a month later. *Id.* at 240-41, 251.

Procedural History

Ms. Rolshoven filed the Petition in this case on May 22, 2014. Pet. at 1. After obtaining affidavits and various relevant medical records from May to December 2014, Petitioner filed such materials followed by a statement of completion on December 12, 2014. ECF No. 17. Respondent thereafter filed his Rule 4(c) Report on February 20, 2015, setting forth his view that Petitioner was not entitled to compensation because she had failed to establish causation. ECF No. 20.

Petitioner filed the first expert report from Dr. Steinman on August 15, 2015, after receiving two extensions of time. ECF No. 24. Respondent then filed his own expert report in response on January 19, 2016, from Dr. Kruer after one extension of time. ECF No. 26. On April 22, 2016, after two additional extensions of time, Petitioner filed a supplemental expert report from Dr. Steinman (ECF No. 30) and Respondent filed his responsive supplemental expert report from Dr. Kruer on August 12, 2016. ECF No. 38.

After the filing of expert reports, I set the matter for hearing on May 11-12, 2017. ECF No. 35. The parties filed prehearing submissions on January 30, 2017, and March 6, 2017, respectively (ECF Nos. 40, 42) and the hearing went forward as scheduled. The parties elected not to file post-hearing briefs. This matter is now ripe for adjudication.

Applicable Legal Standards

A. Petitioner's Overall Burden in Vaccine Program Cases

To receive compensation in the Vaccine Program, a petitioner must prove either: (1) that he suffered a "Table Injury" – *i.e.*, an injury falling within the Vaccine Injury Table – corresponding to one of the vaccinations in question within a statutorily prescribed period of time or, in the alternative, (2) that his illnesses were actually caused by a vaccine (a "Non-Table Injury"). *See* Sections 13(a)(1)(A), 11(c)(1), and 14(a), as amended by 42 C.F.R. § 100.3; §

11(c)(1)(C)(ii)(I); *see also Moberly v. Sec'y of Health & Human Servs.*, 592 F.3d 1315, 1321 (Fed. Cir. 2010); *Capizzano v. Sec'y of Health & Human Servs.*, 440 F.3d 1317, 1320 (Fed. Cir. 2006).[24] In this case, Petitioner does not assert a Table claim.

For both Table and Non-Table claims, Vaccine Program petitioners bear a "preponderance of the evidence" burden of proof. Section 13(1)(a). That is, a petitioner must offer evidence that leads the "trier of fact to believe that the existence of a fact is more probable than its nonexistence before [he] may find in favor of the party who has the burden to persuade the judge of the fact's existence." *Moberly*, 592 F.3d at 1322 n.2; *see also Snowbank Enter. v. United States*, 6 Cl. Ct. 476, 486 (1984) (mere conjecture or speculation is insufficient under a preponderance standard). Proof of medical certainty is not required. *Bunting v. Sec'y of Health & Human Servs.*, 931 F.2d 867, 873 (Fed. Cir. 1991). In particular, a petitioner must demonstrate that the vaccine was "not only [the] but-for cause of the injury but also a substantial factor in bringing about the injury." *Moberly*, 592 F.3d at 1321 (quoting *Shyface v. Sec'y of Health & Human Servs.*, 165 F.3d 1344, 1352-53 (Fed. Cir. 1999)); *Pafford v. Sec'y of Health & Human Servs*., 451 F.3d 1352, 1355 (Fed. Cir. 2006). A petitioner may not receive a Vaccine Program award based solely on his assertions; rather, the petition must be supported by either medical records or by the opinion of a competent physician. Section 13(a)(1).

In attempting to establish entitlement to a Vaccine Program award of compensation for a Non-Table claim, a petitioner must satisfy all three of the elements established by the Federal Circuit in *Althen v. Sec'y of Health & Human Servs.,* 418 F.3d 1274 (Fed. Cir. 2005): "(1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of proximate temporal relationship between vaccination and injury." *Althen,* 418 F.3d at 1278.

Each of the *Althen* prongs requires a different showing. Under *Althen* prong one, petitioners must provide a "reputable medical theory," demonstrating that the vaccine received *can cause* the type of injury alleged. *Pafford*, 451 F.3d at 1355-56 (citations omitted). To satisfy this prong, a petitioner's theory must be based on a "sound and reliable medical or scientific explanation." *Knudsen v. Sec'y of Health & Human Servs.*, 35 F.3d 543, 548 (Fed. Cir. 1994). Such a theory must only be "legally probable, not medically or scientifically certain." *Id.* at 549.

[24] Decisions of special masters (some of which I reference in this ruling) constitute persuasive but not binding authority. *Hanlon v. Sec'y of Health & Human Servs.*, 40 Fed. Cl. 625, 630 (1998). By contrast, Federal Circuit rulings concerning legal issues are binding on special masters. *Guillory v. Sec'y of Health & Human Servs.*, 59 Fed. Cl. 121, 124 (2003), *aff'd* 104 F. App'x 712 (Fed. Cir. 2004); *see also Spooner v. Sec'y of Health & Human Servs.*, No. 13-159V, 2014 WL 504728, at *7 n.12 (Fed. Cl. Spec. Mstr. Jan. 16, 2014).

Petitioners may satisfy the first *Althen* prong without resort to medical literature, epidemiological studies, demonstration of a specific mechanism, or a generally accepted medical theory. *Andreu v. Sec'y of Health & Human Servs.*, 569 F.3d 1367, 1378-79 (Fed. Cir. 2009) (citing *Capizzano*, 440 F.3d at 1325-26). Special masters, despite their expertise, are not empowered by statute to conclusively resolve what are essentially thorny scientific and medical questions, and thus scientific evidence offered to establish *Althen* prong one is viewed "not through the lens of the laboratorian, but instead from the vantage point of the Vaccine Act's preponderant evidence standard." *Id.* at 1380. Accordingly, special masters must take care not to increase the burden placed on petitioners in offering a scientific theory linking vaccine to injury. *Contreras v. Sec'y of Health & Human Servs.*, 121 Fed. Cl. 230, 245 (2015) ("[p]lausibility . . . in many cases *may* be enough to satisfy *Althen* prong one" (emphasis in original)), *vacated on other grounds*, 844 F.3d 1363 (Fed. Cir. 2017). But this does not negate or reduce a petitioner's ultimate burden to establish his overall entitlement to damages by preponderant evidence. *W.C. v. Sec'y of Health & Human Servs.*, 704 F.3d 1352, 1356 (Fed. Cir. 2013) (citations omitted).[25]

The second *Althen* prong requires proof of a logical sequence of cause and effect, usually supported by facts derived from a petitioner's medical records. *Althen*, 418 F.3d at 1278; *Andreu*, 569 F.3d at 1375-77; *Capizzano*, 440 F.3d at 1326; *Grant v. Sec'y of Health & Human Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992). In establishing that a vaccine "did cause" injury, the opinions and views of the injured party's treating physicians are entitled to some weight. *Andreu*, 569 F.3d at 1367; *Capizzano*, 440 F.3d at 1326 ("medical records and medical opinion testimony are favored in vaccine cases, as treating physicians are likely to be in the best position to determine whether a 'logical sequence of cause and effect show[s] that the vaccination was the reason for the injury'") (quoting *Althen*, 418 F.3d at 1280). Medical records are generally viewed as particularly trustworthy evidence, since they are created contemporaneously with the treatment of the patient. *Cucuras v. Sec'y of Health & Human Servs.*, 993 F.2d 1525, 1528 (Fed. Cir. 1993).

However, medical records and/or statements of a treating physician's views do not *per se* bind the special master to adopt the conclusions of such an individual, even if they must be considered and carefully evaluated. Section 13(b)(1) (providing that "[a]ny such diagnosis, conclusion, judgment, test result, report, or summary shall not be binding on the special master or court"); *Snyder v. Sec'y of Health & Human Servs*., 88 Fed. Cl. 706, 746 n.67 (2009) ("there is nothing . . . that mandates that the testimony of a treating physician is sacrosanct – that it must be accepted in its entirety and cannot be rebutted"). As with expert testimony offered to establish a theory of causation, the

[25] Although decisions like *Contreras* suggest that the burden of proof required to satisfy the first *Althen* prong is less than the other two, there is ample contrary authority for the more straightforward proposition that the first *Althen* prong (as a component of the overall test) simply requires application of a preponderance evidentiary standard when evaluating if a reliable and plausible causation theory has been established. *Broekelschen v. Sec'y of Health & Human Servs.*, 618 F.3d 1339, 1350 (Fed. Cir. 2010).

opinions or diagnoses of treating physicians are only as trustworthy as the reasonableness of their suppositions or bases. The views of treating physicians should also be weighed against other, contrary evidence also present in the record – including conflicting opinions among such individuals. *Hibbard v. Sec'y of Health & Human Servs.*, 100 Fed. Cl. 742, 749 (2011) (not arbitrary or capricious for special master to weigh competing treating physicians' conclusions against each other), *aff'd*, 698 F.3d 1355 (Fed. Cir. 2012); *Caves v. Sec'y of Dept. of Health & Human Servs.*, No. 06-522V, 2011 WL 1935813, at *17 (Fed. Cl. Spec. Mstr. Apr. 29, 2011), *mot. for review den'd*, 100 Fed. Cl. 344, 356 (2011), *aff'd without opinion*, 475 Fed. App'x 765 (Fed. Cir. 2012).

The third *Althen* prong requires establishing a "proximate temporal relationship" between the vaccination and the injury alleged. *Althen*, 418 F.3d at 1281. That term has been equated to the phrase "medically-acceptable temporal relationship." *Id.* A petitioner must offer "preponderant proof that the onset of symptoms occurred within a timeframe which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation." *de Bazan v. Sec'y of Health & Human Servs.*, 539 F.3d 1347, 1352 (Fed. Cir. 2008). The explanation for what is a medically acceptable timeframe must also coincide with the theory of how the relevant vaccine can cause an injury (*Althen* prong one's requirement). *Id.* at 1352; *Shapiro v. Sec'y of Health & Human Servs.*, 101 Fed. Cl. 532, 542 (2011), *recons. den'd after remand*, 105 Fed. Cl. 353 (2012), *aff'd mem.*, 2013 WL 1896173 (Fed. Cir. 2013); *Koehn v. Sec'y of Health & Human Servs.*, No. 11-355V, 2013 WL 3214877 (Fed. Cl. Spec. Mstr. May 30, 2013), *mot. for review den'd* (Fed. Cl. Dec. 3, 2013), *aff'd*, 773 F.3d 1239 (Fed. Cir. 2014).

B. Law Governing Analysis of Fact Evidence

The process for making determinations in Vaccine Program cases regarding factual issues begins with consideration of the medical records. Section 11(c)(2). The special master is required to consider "all [] relevant medical and scientific evidence contained in the record," including "any diagnosis, conclusion, medical judgment, or autopsy or coroner's report which is contained in the record regarding the nature, causation, and aggravation of the petitioner's illness, disability, injury, condition, or death," as well as the "results of any diagnostic or evaluative test which are contained in the record and the summaries and conclusions." Section 13(b)(1)(A). The special master is then required to weigh the evidence presented, including contemporaneous medical records and testimony. *See Burns v. Sec'y of Health & Human Servs*., 3 F.3d 415, 417 (Fed. Cir. 1993) (it is within the special master's discretion to determine whether to afford greater weight to contemporaneous medical records than to other evidence, such as oral testimony surrounding the events in question that was given at a later date, provided that such determination is evidenced by a rational determination).

Medical records that are created contemporaneously with the events they describe are presumed to be accurate and "complete" (i.e., presenting all relevant information on a patient's health problems). *Cucuras*, 993 F.2d at 1528; *Doe/70 v. Sec'y of Health & Human Servs.*, 95 Fed. Cl. 598, 608 (2010) ("[g]iven the inconsistencies between petitioner's testimony and his contemporaneous medical records, the special master's decision to rely on petitioner's medical records was rational and consistent with applicable law"), *aff'd*, *Rickett v. Sec'y of Health & Human Servs*., 468 F. App'x 952 (Fed. Cir. 2011) (non-precedential opinion). This presumption is based on the linked propositions that (i) sick people visit medical professionals; (ii) sick people honestly report their health problems to those professionals; and (iii) medical professionals record what they are told or observe when examining their patients in as accurate a manner as possible, so that they are aware of enough relevant facts to make appropriate treatment decisions. *Sanchez v. Sec'y of Health & Human Servs.*, No. 11-685V, 2013 WL 1880825, at *2 (Fed. Cl. Spec. Mstr. Apr. 10, 2013); *Cucuras v. Sec'y of Health & Human Servs.*, 26 Cl. Ct. 537, 543 (1992), *aff'd*, 993 F.2d at 1525 (Fed. Cir. 1993) ("[i]t strains reason to conclude that petitioners would fail to accurately report the onset of their daughter's symptoms.").

Accordingly, if the medical records are clear, consistent, and complete, then they should be afforded substantial weight. *Lowrie v. Sec'y of Health & Human Servs*., No. 03-1585V, 2005 WL 6117475, at *20 (Fed. Cl. Spec. Mstr. Dec. 12, 2005). Indeed, contemporaneous medical records are generally found to be deserving of greater evidentiary weight than oral testimony – especially where such testimony conflicts with the record evidence. *Cucuras*, 993 F.2d at 1528; *see also Murphy v. Sec'y of Health & Human Servs*., 23 Cl. Ct. 726, 733 (1991), *aff'd per curiam*, 968 F.2d 1226 (Fed. Cir. 1992), *cert. den'd*, *Murphy v. Sullivan*, 506 U.S. 974 (1992) (citing *United States v. United States Gypsum Co.*, 333 U.S. 364, 396 (1947) ("[i]t has generally been held that oral testimony which is in conflict with contemporaneous documents is entitled to little evidentiary weight.")).

However, there are situations in which compelling oral testimony may be more persuasive than written records, such as where records are deemed to be incomplete or inaccurate. *Campbell v. Sec'y of Health & Human Servs*., 69 Fed. Cl. 775, 779 (2006) ("like any norm based upon common sense and experience, this rule should not be treated as an absolute and must yield where the factual predicates for its application are weak or lacking"); *Lowrie*, 2005 WL 6117475, at *19 ("[w]ritten records which are, themselves, inconsistent, should be accorded less deference than those which are internally consistent") (quoting *Murphy*, 23 Cl. Ct. at 733)). Ultimately, a determination regarding a witness's credibility is needed when determining the weight that such testimony should be afforded. *Andreu*, 569 F.3d at 1379; *Bradley v. Sec'y of Health & Human Servs*., 991 F.2d 1570, 1575 (Fed. Cir. 1993).

When witness testimony is offered to overcome the presumption of accuracy afforded to contemporaneous medical records, such testimony must be "consistent, clear, cogent, and compelling." *Sanchez*, 2013 WL 1880825, at *3 (citing *Blutstein v. Sec'y of Health & Human Servs*., No. 90-2808V, 1998 WL 408611, at *5 (Fed. Cl. Spec. Mstr. June 30, 1998)). In determining the accuracy and completeness of medical records, the Court of Federal Claims has listed four possible explanations for inconsistencies between contemporaneously created medical records and later testimony: (1) a person's failure to recount to the medical professional everything that happened during the relevant time period; (2) the medical professional's failure to document everything reported to her or him; (3) a person's faulty recollection of the events when presenting testimony; or (4) a person's purposeful recounting of symptoms that did not exist. *La Londe v. Sec'y of Health & Human Servs*., 110 Fed. Cl. 184, 203-04 (2013), *aff'd*, 746 F.3d 1334 (Fed. Cir. 2014). In making a determination regarding whether to afford greater weight to contemporaneous medical records or other evidence, such as testimony at hearing, there must be evidence that this decision was the result of a rational determination. *Burns*, 3 F.3d at 417.

C. Analysis of Expert Testimony

Establishing a sound and reliable medical theory often requires a petitioner to present expert testimony in support of his claim. *Lampe v. Sec'y of Health & Human Servs*., 219 F.3d 1357, 1361 (Fed. Cir. 2000). Vaccine Program expert testimony is usually evaluated according to the factors for analyzing scientific reliability set forth in *Daubert v. Merrell Dow Pharm., Inc.*, 509 U.S. 579, 594-96 (1993). *See Cedillo v. Sec'y of Health & Human Servs.*, 617 F.3d 1328, 1339 (Fed. Cir. 2010) (citing *Terran v. Sec'y of Health & Human Servs.*, 195 F.3d 1302, 1316 (Fed. Cir. 1999). "The *Daubert* factors for analyzing the reliability of testimony are: (1) whether a theory or technique can be (and has been) tested; (2) whether the theory or technique has been subjected to peer review and publication; (3) whether there is a known or potential rate of error and whether there are standards for controlling the error; and (4) whether the theory or technique enjoys general acceptance within a relevant scientific community." *Terran*, 195 F.3d at 1316 n.2 (citing *Daubert*, 509 U.S. at 592-95).

The *Daubert* factors play a slightly different role in Vaccine Program cases than they do when applied in other federal judicial fora (such as the district courts). *Daubert* factors are usually employed by judges (in the performance of their evidentiary gatekeeper roles) to exclude evidence that is unreliable and/or could confuse a jury. In Vaccine Program cases, by contrast, these factors are used in the *weighing* of the reliability of scientific evidence proffered. *Davis v. Sec'y of Health & Human Servs*., 94 Fed. Cl. 53, 66-67 (2010) ("uniquely in this Circuit, the *Daubert* factors have been employed also as an acceptable evidentiary-gauging tool with respect to persuasiveness of expert testimony already admitted"). The flexible use of the *Daubert* factors to evaluate the persuasiveness and reliability of expert testimony has routinely been upheld. *See, e.g.*, *Snyder*, 88

Fed. Cl. at 742-45. In this matter (as in numerous other Vaccine Program cases), *Daubert* has not been employed at the threshold, to determine what evidence should be admitted, but instead to determine whether expert testimony offered is reliable and/or persuasive.

Respondent frequently offers one or more experts to rebut a petitioner's case. Where both sides offer expert testimony, a special master's decision may be "based on the credibility of the experts and the relative persuasiveness of their competing theories." *Broekelschen v. Sec'y of Health & Human Servs*., 618 F.3d 1339, 1347 (Fed. Cir. 2010) (citing *Lampe*, 219 F.3d at 1362). However, nothing requires the acceptance of an expert's conclusion "connected to existing data only by the *ipse dixit* of the expert," especially if "there is simply too great an analytical gap between the data and the opinion proffered." *Snyder*, 88 Fed. Cl. at 743 (quoting *Gen. Elec. Co. v. Joiner*, 522 U.S. 146 91997)); *see also Isaac v. Sec'y of Health & Human Servs*., No. 08-601V, 2012 WL 3609993, at *17 (Fed. Cl. Spec. Mstr. July 30, 2012), *mot. for review den'd*, 108 Fed. Cl. 743 (2013), *aff'd*, 540 Fed. App'x 999 (Fed. Cir. 2013) (citing *Cedillo*, 617 F.3d at 1339). Weighing the relative persuasiveness of competing expert testimony, based on a particular expert's credibility, is part of the overall reliability analysis to which special masters must subject expert testimony in Vaccine Program cases. *Moberly*, 592 F.3d at 1325-26 ("[a]ssessments as to the reliability of expert testimony often turn on credibility determinations"); *see also Porter v. Sec'y of Health & Human Servs*., 663 F.3d 1242, 1250 (Fed. Cir. 2011) ("this court has unambiguously explained that special masters are expected to consider the credibility of expert witnesses in evaluating petitions for compensation under the Vaccine Act").

D. Consideration of Medical Literature

Both parties filed medical and scientific literature in this case, but not all such items factor into the outcome of this decision. While I have reviewed all of the medical literature submitted in this case, I discuss only those articles that are most relevant to my determination and/or are central to Petitioner's case – just as I have not exhaustively discussed every individual medical record filed. *Moriarty v. Sec'y of Health & Human Servs.*, No. 2015-5072, 2016 WL 1358616, at *5 (Fed. Cir. Apr. 6, 2016) ("[w]e generally presume that a special master considered the relevant record evidence even though he does not explicitly reference such evidence in his decision") (citation omitted); *see also Paterek v. Sec'y of Health & Human Servs.,* 527 F. App'x 875, 884 (Fed. Cir. 2013) ("[f]inding certain information not relevant does not lead to – and likely undermines – the conclusion that it was not considered").

ANALYSIS

The parties agree herein that Ms. Huelsenbeck was correctly diagnosed with IIH/PC, and that she did *not* suffer from some form of vasculitis. As a result, some of the expert input in this case was devoted to attacking a straw man, for Petitioner's expert made clear at the hearing that his opinion was not aimed at establishing vasculitis as a vaccine-caused injury which could explain Ms. Huelsenbeck's headaches. (Respondent's points on this subject nevertheless remain salient, because they foreclose certain arguments Dr. Steinman seemed to be making about causation – arguments he abandoned after it was evident they lacked merit).

This leaves Dr. Steinman's effort to propose a theory embracing the record-established facts (which are heavily stacked against Petitioner's claim) but still providing a reliable and plausible causal explanation linking the HPV vaccine to her symptoms. Unfortunately, that effort fell well short of the mark. Petitioner's causation theory has significant reliability problems, and ultimately reflects (as Dr. Steinman repeatedly admitted at hearing) an attempt to craft *some* explanation for how a vaccine might cause the symptoms Ms. Huelsenbeck experienced – regardless of its actual reliability.

I. *Althen* Prong One

Petitioner's causation theory evolved over the course of this litigation, being refined as Respondent weighed in on it. Petitioner (via Dr. Steinman) attempted overall to suggest that headaches such as those experienced by Ms. Huelsenbeck could be caused by the HPV vaccine even if that same vaccine was not deemed the cause of her IIH/PC. But, when Respondent's expert opined (in his first expert report) that what Petitioner was really proposing was that Ms. Huelsenbeck had vasculitis – a diagnosis finding absolutely no support in the record – Petitioner shifted her position, with Dr. Steinman now affirmatively stating that under no circumstances was he so asserting, but that his theory was not diminished by this admission. Tr. at 258-59.

Dr. Steinman was upfront in acknowledging the absence of reliable direct proof connecting the HPV vaccine with PC/IIH, vasculitis, or some other chronic headache syndrome.[26] What remains is a theory that the HPV vaccine could sufficiently "interact," in part via its alum adjuvant, with the cranial blood vessels near the brain to cause headaches separate from Ms. Huelsenbeck's diagnosed IIH, but also not *be* symptomatic of vasculitis, based on strung-together scientific or medical evidence in an attempt to create a circumstantial chain.

[26] Although Dr. Steinman nevertheless maintained that the HPV vaccine's manufacturer recognized a possible link (as reflected in the vaccine package inserts), for the reasons discussed below I give little weight to such purported admissions of a causal relationship (beyond the immediate day or so after vaccination).

There are two separate, equally insurmountable problems with this theory. First, the specific biologic mechanisms proposed under Dr. Steinman's theory are (as applied herein) unreliable.[27] Dr. Steinman proposed one mechanism fully consistent with assertions he makes frequently in other Program cases involving molecular mimicry between protein components of a vaccine (here, the HPV virus) and human peptides, resulting in a cross-reaction where antibodies produced in reaction to the vaccine mistakenly attack self-structures, causing harm. *See Auch v. Sec'y of Health & Human Servs*., No. 12-673V, 2017 WL 1034396 (Fed. Cl. Spec. Mstr. Jan. 13, 2017); *Blackburn v. Sec'y of Health & Human Servs.*, No. 10-410V, 2015 WL 425935 (Fed. Cl. Spec. Mstr. Jan. 9, 2015). His expertise to comment on the biologic process by which this is thought to occur is beyond question – but in this case was not enough to imbue Petitioner's theory with the needed evidentiary heft. For he could muster no reliable evidence that *any* vaccine, let alone the HPV vaccine, has cross-reacted in the manner proposed and in the context of Ms. Huelsenbeck's headaches. At best, Petitioner offered Li, which only identified the presence of genes responsible for expressing MBP in the blood-brain barrier – it did *not* establish that cross-reactions of the sort proposed herein occur there and cause headaches.

Petitioner thus sought to transpose a body of reliable literature involving a biologic mechanism applicable in one circumstance (that infection or vaccination can cause a demyelinating condition involving an autoimmune cross-reaction with the MBP that composes nerve structures) into wholly inapposite circumstances. Petitioner's theory also stretches protein sequence homology as evaluated in the Vaccine Program to its breaking point – and wrongly assumes a showing of homology, uncorroborated by proof that the proposed reaction has been studied and confirmed, is sufficient to prevail. *See Harris v. Sec'y of Health & Human Servs*., No. 10-322V, 2014 WL 3159377, at *17 (Fed. Cl. Spec. Mstr. June 10, 2014), *motion for review denied*, No. 10 10-322V, slip. op. (Fed. Cl. Sept. 24, 2014).

Dr. Steinman's other proposed mechanism - that alum contained in the vaccine would sufficiently stimulate cytokine-induced inflammation in cranial blood vessels to cause headaches - is equally deficient. The evidence he offered to suggest alum's role largely consisted of general literature discussing how alum functions as an immunologic booster – but does not establish that alum can cause the upregulation of cytokines in a pathogenic matter, let alone produce the chronic headaches experienced by Ms. Huelsenbeck. I have previously addressed the deficiencies and

[27] It is well-recognized that claimants need not establish a biologic mechanism to prevail – but when they attempt to do so (especially in cases like this, where there is an absence of direct evidence associating the relevant vaccine with the alleged injury), a special master may evaluate how successful that effort has been, weighing the evidentiary showing pertaining to the proposed mechanism against the other evidence offered for Petitioner's claim, and/or evidence offered in rebuttal by Respondent. *W.C.*, 704 F.3d 1352; *Crutchfield v. Sec'y of Health & Human Servs.,* No. 09-0039V, 2014 WL 1665227, at*13-15 (Fed. Cl. Spec. Mstr. Apr. 7, 2014).

unpersuasive character of this theory in cases in which claimants offered far more extensive literature in support of it than herein. *See, e.g.*, *Olson v. Sec'y of Health & Human Servs.,* No. 13-439V, 2017 WL 3624085, at *20-21 (Fed. Cl. Spec. Mstr. July 14, 2017) (insufficiently reliable scientific or medical evidence to support contention that alum used as adjuvant in HPV vaccine could trigger autoimmune process resulting in rheumatoid arthritis), *mot. for review den'd*, 2017 WL 6809589 (Fed. Cl. Dec. 14, 2017).

Second, Petitioner's causation theory is greatly constrained by the indisputable facts pertaining to Ms. Huelsenbeck's diagnosis. The medical record incontrovertibly shows that she was properly diagnosed with IIH/PC, and that *this* condition accounted for most of her chronic headaches, which were in turn resolved by treatment targeted for the condition. At the same time, there is no evidence of vasculitis (and Dr. Steinman was emphatic in asserting this was *not* an element of his theory). Dr. Steinman was therefore reduced to attempting to argue that *some* of the headaches that a person properly diagnosed with IIH could be caused by the HPV vaccine in a vasculitis-like presentation (despite the absence of vasculitis). But he had almost no reliable scientific or medical evidence to support his attempt to differentiate between types of headaches, or to relate some vasculitis-like presentations to the HPV vaccine. Indeed, articles such as Tomljenovic (which suggests a link between HPV vaccine and vasculitis) were not only demonstrated by Respondent to be unreliable, but also were admitted by Dr. Steinman to have low probative value herein (Tr. at 114) – *and* involved a condition that Dr. Steinman expressly disavowed as pertinent to his theory.

Dr. Steinman's points about disclosures contained in the HPV package insert warning of the possibility of post-vaccine headaches are also unpersuasive. As I have previously observed in other cases, vaccine package inserts do not constitute causation evidence meriting significant weight. *Sullivan v. Sec'y of Health & Human Servs.,* No. 10-398, 2015 WL 1404957, at*20 (Fed. Cl. Spec. Mstr. Feb. 13, 2015)("[s]tatements contained in vaccine package inserts do not constitute reliable proof of causation, and cannot be deemed admissions that the vaccines in question have the capacity to harm a particular petitioner in a specific manner"); *see also Werderitsh v. Sec'y of Health & Human Servs.*, No. 99–319V, 2005 WL 3320041, at *8 (Fed. Cl. Spec. Mstr. Nov. 10, 2005) (quoting 21 C.F.R. § 600.80(l) as saying "[a] report or information submitted by a licensed manufacturer . . . does not necessarily reflect a conclusion by the licensed manufacturer or FDA that the report or information constitutes an admission that the biological product caused or contributed to an adverse effect").

Besides the substantive deficiencies of Petitioner's causation theory, the theory's persuasiveness was significantly undermined by Dr. Steinman's numerous asides during the hearing regarding his role as expert. Perhaps in tacit recognition that his theory lacked scientific or medical reliability, Dr. Steinman repeatedly proposed that his primary task was to offer the best

theory he could string together from available medical literature. *See, e.g.*, Tr. at 39. Implicit in such statements was an admission: that the overall scientific or medical reliability of his opinion mattered less than his good faith in striving to come up with *something* that might conceivably help Petitioner succeed. But this characterization of the expert's role – not only in the Vaccine Program but in any disputed matter in a federal court – is misguided.[28]

Dr. Steinman's metaphor for crossing a river, stone to stone, in proposing a causation theory, was apt – but in this case, he fell into that river and never reached the other side.

II. *Althen* Prong Two

Besides the apparent deficiencies in Petitioner's theory discussed above, the claim asserted herein fails also because the medical record is inconsistent with that theory. There is no evidence in the record of any post-vaccine reaction to either the second or third HPV doses. There is no evidence either of inflammation, whether indirectly (as observed in CSF testing) or in the classic sense, despite Dr. Steinman's theory of cross-reaction involving the HPV vaccine. Tr. at 129. There were no other findings or test results that would suggest an autoimmune process was underway. And nothing from the record helps to distinguish between IIH-associated headaches and headaches occurring in accordance with Dr. Steinman's theory (beyond the fact that Ms. Huelsenbeck did experience some additional headaches even after her IIH was successfully treated).

Also, treater support for Petitioner's theory is undercut by the overall record. Thus, although Ms. Huelsenbeck's primary care provider, Dr. Hartberg, did at one point speculate that the HPV vaccine might have had some relationship to her headaches, he did so before she was seen by Dr. Tseng, who correctly diagnosed her IIH and treated it effectively. Once her condition was treated in the proper manner, Ms. Huelsenbeck's headaches mostly resolved. The return of headaches some months later, given the lack of corroborative support for Petitioner's theory,

[28] In discussing my misgivings about these asides, it is not my intent to impugn Dr. Steinman's character or honesty. I have had the opportunity to hear his testimony numerous times, and he has repeatedly impressed me as an exceedingly qualified and intelligent expert, with knowledge particularly suited to Vaccine Program claims. But his overfamiliarity with the Program (and particularly its adjudicative procedures and applicable legal standards) may have led him astray in this instance. It is reasonable for me to draw conclusions about whether such statements, made under oath in this proceeding, impacted the persuasiveness of his opinion in this case, in keeping with my duty as a special master to weigh competing expert testimony. *See Copenhaver v. Sec'y of Health & Human Servs.*, No. 13-1002V, 2016 WL 6947389, at *5 (Fed. Cl. Oct. 20, 2016) ("Special Masters may use their discretion in weighing expert testimony, and case law supports that discretion"); *Porter v. Sec'y of Health & Human Servs*., 663 F.3d 1242, 1250 (Fed. Cir. 2011) ("This court has unambiguously explained that special masters are expected to consider the credibility of expert witnesses in evaluating petitions for compensation under the Vaccine Act").

cannot be explained, but it also cannot be attributed to the reaction Petitioner proposes absent other corroborative proof.

The disparate factual occurrences after Ms. Huelsenbeck received the second and third HPV doses further illustrate the evidentiary failures that make it impossible to conclude in this case that the HPV vaccine "did cause" her headaches. Dr. Steinman testified that certain vaccines such as HPV are administered in a series of doses in order to guarantee a robust response. Tr. at 56. As a result (and in accordance with the concept of "challenge-rechallenge"),[29] to be consistent with Petitioner's theory, Ms. Huelsenbeck's response to the third dose should have been swifter and more severe. *Id.* at 58 (Dr. Steinman summarizing challenge-rechallenge as "the more times you see something, the stronger the recall response and the more rapid the immunological memory kicks in"). Yet in this case, although Ms. Huelsenbeck reported headaches within ten days of the second dose, she reported *no* headaches until a month after the third.[30] Ex. 2 at 8, 11. No explanation was provided by Petitioner or her expert for why the time period was longer after the third dose, when a shorter time period would be expected.

III. *Althen* Prong Three

My determination that preponderant evidence does not support Petitioner's causation theory obviates the need to evaluate if the timing of Ms. Huelsenbeck's headaches after vaccination was medically acceptable. *See, e.g., Lasnetski v. Sec'y of Health & Human Servs.*, 128 Fed. Cl. 242, 64 (2016), *aff'd*, 696 Fed. App'x 497 (2017). But just as the medical record does not corroborate Petitioner's theory, it also provides no real support for this prong of the *Althen* test either. There is no clear relationship between the onset of Ms. Huelsenbeck's headaches after the second versus third HPV doses that would permit the conclusion that the overall timeframe in which her injuries unfolded is acceptable. Indeed, the third dose was only temporally followed by additional headaches a month later – but so was the PC/IIH diagnosis. And when Petitioner's IIH was treated, her headaches almost completely subsided. Petitioner has not provided a persuasive and medically reliable narrative explaining the HPV vaccine's role in her up-and-down headache course. At the same time, her treaters identified a cause for her condition (at least after the third

[29] Challenge-rechallenge is "a paradigm for exploring whether a substance caused an adverse reaction. Under this model, an individual who has had an adverse reaction to an initial vaccine dose (the challenge event) suffers a worsening of symptoms after a second or third injection (the rechallenge event)," thereby establishing the vaccine's causal role. *Viscontini v. Sec'y of Health & Human Servs.*, No. 98-619V, 2011 WL 5842577, at *22 (Fed. Cl. Spec. Mstr. Oct. 21, 2011) (quoting *Doe/70 v. Sec'y of Health & Human Servs.*, 95 Fed. Cl. 598, 603 (2010) (quotations omitted)), *mot. for review den'd,* 103 Fed. Cl. 600 (2012).

[30] I also note in passing that Petitioner alleges Ms. Huelsenbeck experienced no reaction at all to the first dose, further reducing the possibility that she experienced any reaction at all to the HPV vaccine.

dose) supported by the record. And Dr. Steinman's opinions on the appropriateness of onset timing in this case relied too heavily on other diseases and other vaccines.

CONCLUSION

I have sympathy for the difficulties the Rolshoven family experienced in its unstinting efforts to care for Ms. Huelsenbeck, and do not doubt that this claim was brought in a good-faith belief that the HPV vaccine might have something to do with her symptoms. But good intentions are not enough in the Vaccine Program, in the absence of persuasive record or scientific proof. And expert opinions must possess a reliable scientific foundation. That has not been accomplished in this case, and therefore I DISMISS this claim.

In the absence of a timely-filed motion for review (see Appendix B to the Rules of the Court), the Clerk shall enter judgment in accord with this decision.[31]

IT IS SO ORDERED.

/s/ Brian H. Corcoran
Brian H. Corcoran
Special Master

[31] Pursuant to Vaccine Rule 11(a), the parties may expedite entry of judgment by filing a joint notice renouncing their right to seek review.